

Amendments to the Claims

1. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the riboswitch regulates expression of the sequence via dynamic interplay between the aptamer domain and the expression platform domain resulting in allosteric control of expression of the sequence, wherein the riboswitch and sequence are heterologous, wherein the sequence does not encode β -galactosidase.

2. (Currently Amended) The construct of claim 1 ~~wherein the riboswitch comprises an aptamer domain and an expression platform domain~~, wherein the aptamer domain and the expression platform domain are heterologous.

3. (Currently Amended) The construct of claim 1 ~~wherein the riboswitch comprises an aptamer domain and an expression platform domain~~, wherein the aptamer domain comprises a P1 stem, wherein the P1 stem comprises an aptamer strand and a control strand, wherein the expression platform domain comprises a regulated strand, wherein the regulated strand, the control strand, or both have been designed to form a stem structure.

4. (Currently Amended) A riboswitch, wherein the riboswitch is a non-natural derivative of a naturally-occurring riboswitch, wherein the riboswitch is not derived from a naturally-occurring adenosylcobalamin-responsive riboswitch.

5. (Original) The riboswitch of claim 4 wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain and the expression platform domain are heterologous.

6. (Currently Amended) The riboswitch of claim 4 wherein the riboswitch is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, ~~adenosylcobalamin-responsive riboswitch~~, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

7. (Original) The riboswitch of claim 4 wherein the riboswitch is activated by a trigger molecule, wherein the riboswitch produces a signal when activated by the trigger molecule.

Claims 8-19. (Canceled).

20. (Currently Amended) The construct of ~~claim 1~~claim 2, wherein the expression platform domain comprises an expression regulatory element.

21. (Previously Presented) The construct of claim 20, wherein the expression regulatory element is selected from the group comprising Shine-Dalgarno sequences, initiation codons, transcription terminators, and stability and processing signals.

Claims 22 to 45 (Not entered).

46. (Currently Amended) The construct of claim 1, ~~wherein the riboswitch comprises an aptamer domain and an expression platform domain~~, wherein the aptamer domain does not control a ribozyme.

47. (Previously Presented) The construct of claim 1, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain comprises a P1 stem, wherein the P1 stem comprises an aptamer strand and a control strand, wherein the expression platform domain comprises a regulated strand, wherein the regulated strand, the control strand, or both have been designed to form a stem structure,

wherein the riboswitch is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

48. (Previously Presented) The construct of claim 47, wherein the riboswitch is a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

49. (Previously Presented) The construct of claim 47, wherein the derivative of the naturally-occurring riboswitch consists of only base pair conservative changes of the naturally-occurring riboswitch.

50. (Previously Presented) The construct of claim 1, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain comprises a

P1 stem, wherein the P1 stem comprises an aptamer strand and a control strand, wherein the expression platform domain comprises a regulated strand, wherein the regulated strand, the control strand, or both have been designed to form a stem structure,

wherein the aptamer domain is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

51. (Previously Presented) The construct of claim 50, wherein the aptamer domain is the aptamer domain of a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

52. (Previously Presented) The construct of claim 50, wherein the derivative of the naturally-occurring riboswitch consists of only base pair conservative changes of the naturally-occurring riboswitch.

53. (Previously Presented) The construct of claim 1, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain comprises a P1 stem, wherein the P1 stem comprises an aptamer strand and a control strand, wherein the expression platform domain comprises a regulated strand, wherein the regulated strand, the control strand, or both have been designed to form a stem structure,

wherein the expression platform domain is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

54. (Previously Presented) The construct of claim 53, wherein the expression platform domain is the expression platform domain of a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

55. (Previously Presented) The construct of claim 53, wherein the derivative of the naturally-occurring riboswitch consists of only base pair conservative changes of the naturally-occurring riboswitch.

56. (Previously Presented) The construct of claim 1, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain comprises a P1 stem, wherein the P1 stem comprises an aptamer strand and a control strand, wherein the expression platform domain comprises a regulated strand, wherein the regulated strand, the control strand, or both have been designed to form a stem structure,

wherein the aptamer domain is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch,

wherein the expression platform domain is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

57. (Previously Presented) The construct of claim 56, wherein the aptamer domain is the aptamer domain of a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch,

wherein the expression platform domain is the expression platform domain of a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch.

58. (Previously Presented) The construct of claim 56, wherein the derivative of the naturally-occurring riboswitch consists of only base pair conservative changes of the naturally-occurring riboswitch.

59. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11A.

60. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11B.

61. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11C.

62. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11D.

63. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11E.

64. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11F.

65. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 11G.

66. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 14A.

67. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 19A.

68. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 24A.

69. (Previously Presented) The construct of claim 1, wherein the riboswitch has the consensus structure of Figure 30A.

70. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the riboswitch regulates expression of the sequence, wherein the aptamer domain does not control a ribozyme, wherein the riboswitch and sequence are heterologous, wherein the sequence does not encode β -galactosidase.

71. (Previously Presented) The construct of claim 70, wherein the riboswitch regulates expression of the sequence.

72. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence encoding a protein or peptide of interest, wherein the riboswitch regulates expression of the protein or peptide of interest, wherein the riboswitch and sequence encoding the protein or peptide of interest are heterologous, wherein the sequence does not encode β -galactosidase, wherein the riboswitch is derived from a naturally-occurring riboswitch.

73. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch regulates transcription, translation, or both transcription and translation of the sequence, wherein the riboswitch and sequence are heterologous, wherein the sequence does not encode β -galactosidase, wherein the riboswitch is derived from a naturally-occurring riboswitch.

74. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence encoding a protein or peptide of interest, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the riboswitch regulates expression of the sequence, wherein the riboswitch and the sequence encoding the protein or peptide of interest are heterologous, wherein the aptamer domain does not control a ribozyme, wherein the sequence does not encode β -galactosidase.

75. (Previously Presented) The construct of claim 74, wherein the riboswitch regulates expression of the sequence.

76. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a coding region, wherein the coding region encodes a protein, wherein the riboswitch regulates expression of the protein, wherein the riboswitch and coding region are heterologous, wherein the coding region does not encode β -galactosidase, wherein the riboswitch is derived from a naturally-occurring riboswitch.

77. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a coding region, wherein the riboswitch regulates expression of the coding region, wherein the riboswitch and coding region are heterologous, wherein the coding region does not encode β -galactosidase, wherein the riboswitch is derived from a naturally-occurring riboswitch.

78. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch regulates expression of the sequence, wherein the riboswitch and sequence are heterologous, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer domain is a naturally-occurring aptamer, wherein the sequence does not encode β -galactosidase.

79. (Currently Amended) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch regulates expression of the sequence, wherein the riboswitch and sequence are heterologous,

wherein the riboswitch is derived from a naturally-occurring guanine-responsive riboswitch, adenine-responsive riboswitch, lysine-responsive riboswitch, thiamine pyrophosphate-responsive riboswitch, adenosylcobalamin-responsive riboswitch, flavin mononucleotide-responsive riboswitch, or a S-adenosylmethionine-responsive riboswitch,

wherein the derivative of the naturally-occurring riboswitch consists of only base pair conservative changes of the naturally-occurring riboswitch, wherein the sequence does not encode β -galactosidase.

80. (Previously Presented) The construct of claim 1, wherein the sequence comprises a coding region.

81. (Previously Presented) The construct of claim 1, wherein the sequence encodes a protein or peptide of interest.

82. (Previously Presented) The construct of claim 1, wherein the sequence comprises an expression product.

83. (Previously Presented) The construct of claim 1, wherein the sequence is a heterologous sequence.

84. (New) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer changes state or structure when bound by a trigger molecule, wherein the expression platform domain changes state or structure when the aptamer domain changes state or structure, wherein the riboswitch regulates expression of the sequence, wherein the riboswitch and sequence are heterologous, wherein the sequence does not encode β -galactosidase.

85. (New) The construct of claim 84, wherein the change of state or structure of the expression platform domain comprises a change in base pairing of nucleotides in the expression platform domain.

86. (New) The construct of claim 84, wherein the change of state or structure of the aptamer domain comprises a change in base pairing of nucleotides in the aptamer domain upon binding the trigger molecule.

87. (New) The construct of claim 84, wherein the change of state or structure of the expression platform domain comprises formation of an alternative stem structure.

88. (New) The construct of claim 84, wherein binding of the aptamer domain by the trigger molecule results in allosteric control of expression of the sequence via interaction of the aptamer domain and the expression platform domain.

89. (New) The construct of claim 1, wherein binding of the aptamer domain by the trigger molecule results in allosteric control of expression of the sequence via interaction of the aptamer domain and the expression platform domain.

90. (New) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the riboswitch regulates expression of the sequence via dynamic interplay between the aptamer domain and the expression platform domain resulting in allosteric control of expression of the sequence, wherein

the aptamer domain and the expression platform domain are heterologous, wherein the sequence does not encode β -galactosidase.

91. (New) A regulatable gene expression construct comprising a nucleic acid molecule encoding an RNA comprising a riboswitch operably linked to a sequence, wherein the riboswitch comprises an aptamer domain and an expression platform domain, wherein the aptamer changes state or structure when bound by a trigger molecule, wherein the expression platform domain changes state or structure when the aptamer domain changes state or structure, wherein the riboswitch regulates expression of the sequence, wherein the aptamer domain and the expression platform domain are heterologous, wherein the sequence does not encode β -galactosidase.